REMARKS

Objections to the claims

The Examiner indicates that the objections to claims 2 and 3 have been withdrawn, but that the objections would be reinstated if the terms "both" and "all of the" were deleted from the claims.

Rejection of the claims under 35 U.S.C. §112, first paragraph

Claim 6 has been rejected under 35 U.S.C. §112, first paragraph with the assertion that the specification does not provide support for amended feature of "which inhibits Fas-mediated apoptosis." The Examiner indicates that Applicants have not drawn to the Examiner's attention to the page and line number where support may be found. Applicants traverse this rejection and withdrawal thereof is respectfully requested.

The Examiner is requested review the page 10, final sentence of the amendment of August 22, 2001, wherein Applicants stated that support for the amendments to claim 6 may be found in the specification on page 13, line 1 through page 14, line 20 and page 41, line 5 through page 42, line 8. The Examiner attention is specifically directed to page 14, lines 7-20 and page 41, lines 5-18. For example page 14, lines 10-12 state, "the soluble Fas ligand functions as a Fas antagonist or as an apoptosis regulator to suppress, inhibit, or regulate the apoptosis." *(emphasis added)* In addition, page 14, lines 14-16 state, "Use of the soluble Fas ligand of the present invention which

functions as a Fas antagonist has enabled to treat and prevent the FasL-induced apoptosis." Thus, the amendment to claim 6 is fully supported by the disclosure of the specification and withdrawal of the rejection is respectfully requested.

Rejections under 35 U.S.C. §112, second paragraph

Claims 2, 3, 5, 8, 10 and 11 have been rejected under 35 U.S.C. §112, second paragraph as being indefinite. More specifically, the Examiner asserts that claims 2, 3, 10 and 11 are indefinite in the recitation of "at least one amino acid residue of from 111^{th} amino acid to 128^{th} amino acid residues." Claims 2, 3, 10 and 11 have been amended pursuant to the suggestion of the Examiner to recite, "at least one amino acid residue from 111^{th} amino acid to 128^{th} amino acid residues." Withdrawal of the rejection is respectfully requested.

Rejections under 35 U.S.C.§102

Claims 2 and 5 have been rejected under 35 U.S.C. §102 as being anticipated by U.S. Pat. No. 6,183,951. The Examiner asserts that U.S. No. '951 contains a human Fas ligand sequence wherein residues 129 and 130 from the N-terminal end are both substituted and at least one amino acid from the 111^{th} to 128^{th} amino acid residues and 131^{st} to 133^{rd} amino acid residues as measured from the N-terminal end are substituted. The Examiner specifically points to Sequence 14 of U.S. No. '951 as being identical to the sequence of claim 2 of the present application,

as well as Sequence Nos. 11 and 13. Applicants traverse this rejection and withdrawal thereof is respectfully requested.

Claim 2 recites the feature that the polypeptide of the invention has an amino acid sequence of natural human Fas ligand wherein

the 129th amino acid and 130th amino acid residues are both deleted or substituted, and

at least one amino acid residue from the 111th amino acid to 128th amino acid residues or at least one amino acid residue from the 131st amino acid to 133rd amino acid residues is deleted or substituted. Thus, one feature of the invention of claim 2 is that the polypeptide has an amino acid sequence of natural human Fas ligand.

The polypeptide of Sequence 14 of U.S. No. '591 is not identical to the sequence of claim 2 nor does the polypeptide of Sequence 14 have an amino acid sequence of natural human Fas ligand. The differences in the sequences can be seen from the alignment of Sequence 14 and the invention of claim 2 found on the final page of the data sheet pages attached to the Office Action. The alignment on the final page shows that the "Best Local Similarity" between Qy (the amino acid sequence of the present invention inputted by the Examiner into the query) and Db (Sequence 14 of U.S. No. '591) is 27.9%. One skilled in the art would not consider a peptide having a homology of only 27.9% to be a polypeptide having the amino acid sequence of natural human FasL. As such, Sequence 14 of US No. '591 does not fall within

the scope of claim 2 and does not anticipate the subject matter of the present invention.

In addition, the DNA sequences of SEQ ID NOS:11 and 13 of U.S. No. '591 correspond respectively to wild-type TNF-β and mutant TNF-β (see column 3, lines 53-58). As such, the DNA of SEQ ID NOS: 11 and 13 of U.S. No. '591 do not encode a FasL and the reference does not disclose the DNA of claim 5 coding for a peptide of claim 2 of the present application. Thus, the invention of claims 2 and 5 is not anticipated by the disclosure of U.S. No. '591 and withdrawal of the rejection is respectfully requested.

As the above-indicated amendments and remarks address and overcome the objections and rejections of the specification and claims, withdrawal of the objections and rejections and allowance of the claims are respectfully requested.

Should the Examiner have any questions regarding the above-indicated application she is requested to please contact MaryAnne Armstrong, PhD (Reg. No. 40,069) in the Washington DC area at (703) 205-8000.

A marked-up version of the specification and claims showing amendments is attached hereto.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any

overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

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Attachment: Version with Markings to Show Changes Made

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS

Claims 2, 3, 10 and 11 have been amended as follows.

2. A novel polypeptide having an amino acid sequence of natural human Fas ligand wherein the 129th amino acid and 130th amino acid residues as measured from N terminal end are both deleted or substituted, and at least one amino acid residue ~~of~~ from 111th amino acid to 128th amino acid residues or at least one amino acid residue ~~of~~ from 131st amino acid to 133rd amino acid residues as measured from N terminal end is deleted or substituted.

3. A novel polypeptide having an amino acid sequence of natural human Fas ligand wherein all of the 8th amino acid to 69th amino acid residues as measured from N terminal end are deleted, 129th amino acid and 130th amino acid residues as measured from N terminal end are both deleted or substituted, and at least one amino acid residue ~~of~~ from 111th amino acid to 128th amino acid residues or at least one amino acid residues from 131st amino acid to 133rd amino acid residues as measured from N terminal end is deleted or substituted.

10. A novel polypeptide having an amino acid sequence of natural human Fas ligand wherein the 129th amino acid and 130th amino acid residues as measured from N terminal end are both

deleted or substituted, and at least one amino acid residue ~~of~~ from 111^{th} amino acid to 128^{th} amino acid residues or at least one amino acid residue ~~of~~ from 131^{st} amino acid to 133^{rd} amino acid residues as measured from N terminal end is deleted or substituted, wherein said novel polypeptide has membrane binding activity and induces Fas-mediated apoptotic activity.

11. A novel polypeptide having an amino acid sequence of natural human Fas ligand wherein all of the 8^{th} amino acid to 69^{th} amino acid residues as measured from N terminal end are deleted, 129^{th} amino acid and 130^{th} amino acid residues as measured from N terminal end are both deleted or substituted, and at least one amino acid residue ~~of~~ from 111^{th} amino acid to 128^{th} amino acid residues or at least one amino acid residues from 131^{st} amino acid to 133^{rd} amino acid residues as measured from N terminal end is deleted or substituted wherein said novel polypeptide has membrane binding activity and induces Fas-mediated apoptotic activity.